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**Genetic and Environmental Influences on Developmental Milestones and
Movement: Results From the Gemini Cohort Study**

Conflict of interest declared: None

Running title: Developmental motor milestones

KEYWORDS: Activity; child; motor; twin

Abstract

Purpose: Variability in the timing of infant developmental milestones is poorly understood. We used a twin analysis to estimate genetic and environmental influences on motor development and activity levels in infancy.

Method: Data were from the Gemini Study, a twin birth cohort of 2,402 families with 10 twins born in the United Kingdom in 2007. Parents reported motor activity level for each of the twins at age 3 months using the Revised Infant Behavior Rating Scale and reported the ages at which they first sat unsupported, crawled, and walked unaided.

Results: Activity level at 3 months and ages when first sitting and crawling were about equally influenced by the shared family environment (45%–54%) and genes (45%–48%). Genetic influences dominated for age when children took their first independent 15 steps (84%).

Conclusion: Aspects of the shared family environment appear to be important influences on motor activity levels and early milestones, although the timing of walking may have a stronger genetic influence. Further research to identify the specific environmental and genetic factors that promote early activity may be important for longer-term health outcomes.

Introduction

The foundations of an active lifestyle are laid in early infancy, with evidence that the age of achieving developmental milestones in infancy is related to future sports participation (Ridgeway et al., 2009). Motor milestones have also been associated with critical transitions, such as school readiness (Cowen, Work, Wyman, & Jarrell, 1994), and with educational outcomes throughout life

(Taanila, Murray, Jokelainen, Isohanni, & Rantakillio, 2005). Age of attainment of early developmental milestones is important evidence for parents and pediatricians that infants are developing normally.

Conventional cohort studies have not been designed to distinguish environmental from genetic effects, but studies of twins make it possible to obtain quantitative estimates of genetic and environmental influences (Plomin, DeFries, McLean, & McGuffin, 2008). Several smaller twin studies have examined infant activity level (e.g., movement of arms and legs, squirming). In a sample of 302 pairs of twins aged 3 months to 16 months old, genetic factors explained 55% of the variance in infant activity level and the unique environment (which includes measurement error) explained the remainder (Goldsmith & Campos, 1999). In 60 pairs of twins, monozygotic (MZ) correlations were higher than dizygotic (DZ) correlations for both parent-rated and objectively measured infant activity level, suggesting genetic influence (Saudino & Eaton, 1991). However, larger samples are needed to distinguish shared and nonshared environmental effects.

Few twin studies have examined the age of attaining milestones such as sitting unsupported, crawling, or walking unaided, and results have been inconsistent.

One study involving 626 siblings and 98 pairs of twins revealed that shared environmental influences explained more than half the variance in ages when sitting without support, turning over, and walking five steps unaided (Peter, Vainder, & Livshits, 1999). In contrast, in a sample of 84 pairs of twins,

genetic factors explained the majority of the variation in ages when sitting, crawling, and standing (Goetghebuer et al., 2003). This variability is likely a consequence of limited sample sizes.

The present study used data from a large, population-based twin cohort (n = 4,804 children) to assess genetic and environmental influences on movement activity level and three important developmental milestones in infancy: first sitting unsupported, first crawling, and first steps.

Method

Gemini Study and participants

The Gemini Study included a cohort of twins born in the United Kingdom in 2007 and was designed to assess genetic and environmental influences on growth and development (van Jaarsveld, Johnson, Llewellyn, & Wardle, 2010). Half of all families with twins born in England and Wales during the recruitment period

(March 2007–December 2007) agreed to be contacted about the study (n = 3,435). Families in which there had been a death were not contacted. Just less than 40%

(n = 2,402) returned the baseline questionnaire when twins were around 8.2 months old (SD = 2.2 months, range 4.0–20.3 months). The first follow-up questionnaire was completed by 1,931 families (80.4% of the baseline sample), when twins were 15.8 months old (SD = 1.1, 85 range = 14.0–27.4 months). Participants classified their own ethnicity. Opposite-sex twins were classified as DZ. Parents of same-sex twins were asked to complete a set of

20 questions validated against polymorphic DNA markers (Price et al., 2000) to determine whether the twins were MZ or DZ. Zygosity was uncertain for 68 pairs, who were excluded from these analyses. Each pair of twins was raised in the same environment.

Comparisons with national twin statistics (Office for National Statistics, 2006) indicated that the Gemini cohort is representative of UK twins in sex, zygosity distribution, gestational age at birth, and birth weight (van Jaarsveld et al., 2010). Gemini parents tended to be slightly healthier than the general population in terms of fruit and vegetable intake, smoking rates, and body mass index, and the majority were White-British and married (van Jaarsveld et al., 2010). Parents who did not complete the follow-up questionnaire were slightly younger (Mage = 32 years, SD = 5 years vs. Mage = 34 years, SD = 5 years; $p < .001$), had slightly lower educational qualifications Q2 (2.9, SD = 1.9 vs. 3.6 SD = 1.9; $p < .001$), and were more likely to be from a Non-White ethnic group ($p < .001$). All parents provided informed consent. The University College London Committee of Non-National Health Service Human Research granted ethical approval.

Infant movement activity level

Infant movement activity level was assessed in the baseline questionnaire using a subscale from the Revised Infant Behavior Questionnaire (IBQ-R; Gartstein & Rothbart, 2003). The IBQ-R is widely used in developmental research, and the Activity subscale has demonstrated good reliability and validity (Gartstein & Rothbart, 2003). Parents were asked to think about each

child's behavior in the first 3 months of life and report on several aspects (e.g., "During feeding, how often did your babies squirm or kick?"; "During sleep, how often did your babies toss about in the crib?"; "When placed in a seat, did your babies wave or kick their arms?") using a 5-point Likert scale ("very rarely"; "less than half the time"; "about half the time"; "more than half the time"; "almost always"). An overall infant movement activity level score was calculated for each child, with higher scores indicating higher levels. Where five or more values were missing, data were excluded from analyses (n = 120 children), leaving a total of 2,274 pairs of twins. The IBQ-R in Gemini demonstrated good internal consistency (Cronbach's alpha = .85).

Early motor milestones

Parents were asked a series of questions, and in each case, they responded separately for the first-born and second-born twins: "How old were your twins when they could sit up without being supported?"; "How old were your twins when they could first crawl on hands and knees?"; "How old were your twins when they could take a few steps without any support?" Parents also had the option to select "not yet." We asked about twins' first sit and first crawl in both the baseline and 15-month questionnaires; we only asked about first steps in the 15-month questionnaire. If parents responded to the sit and crawl questions on both occasions and there was a discrepancy of more than 2 months between values, data were counted as missing. Where responses were different by 2 months or less, values from the baseline questionnaire were used, but results were checked using the 15-month data and there were

no differences. A few children had not yet reached each milestone by the time the 15-month questionnaire was returned (first sit, 0.6%; first steps, 23%), and 2% of children were “noncrawlers.” The exact numbers of infants included are provided in the “Results” section.

Statistical analyses

Associations between infant movement activity level and developmental milestones were assessed using partial correlations adjusting for gestational age. For twin analyses, data were regressed on age (gestational age and age of twins at questionnaire completion) and sex. Residuals from regressions were used for all analyses. Within-pair intraclass correlation coefficients (ICCs) were computed to provide preliminary evidence of genetic influence, based on the assumption that MZ (identical) twins share all of their genes and DZ (fraternal) twins share on average half their segregating genes. If a trait is purely genetic, MZ twins would be perfectly correlated (1.0) and the DZ correlation would be .5. Intraclass correlation coefficients were computed using the Statistical Package for the Social Sciences software.

Structural equation modeling was used to generate quantitative estimates of additive genetic effects (A), shared environment effects (C), and unshared environment effects plus measurement error (E) using MX maximum likelihood structural equation modeling software (Version 32, Virginia Commonwealth University, Richmond, VA). Parsimony of submodels (CE, AE, and E) was tested with two goodness-of fit-statistics: change in χ^2 and Akaike’s information criteria. Post-hoc power calculations were conducted in

MX. To test for contrast effects, MZ and DZ correlations were examined and equal variance by zygosity was tested (Levine's test). Significance was set at $\alpha < .05$.

Results

Participant characteristics are presented in Table 1. There were no significant differences between MZ and DZ twins in age at time of questionnaire completion, infant movement activity level, or age at first steps (all p s $> .05$). Age at first sit was slightly later in MZ twins than DZ twins, with a mean difference of 0.34 months (95% confidence interval [CI] [0.12, 0.39]; $d = 0.216$), as was first crawl, with a mean difference of 0.25 months (95% CI [0.12, 0.39]; $p < .001$; $d = 0.133$).

Correlations between infant movement activity level and developmental milestones are presented in Table 2. There was a low correlation ($r = -.212$, $p < .001$) between higher infant movement activity level and first crawl at a younger age, although there was no correlation between higher infant movement activity level and first sit ($r = -.168$, $p < .001$) or first steps ($r = -0.135$, $p < .001$) at a younger age. There were moderate correlations between first sit and first crawl ($r = .468$, $p < .001$) and between first crawl and first steps ($r = .476$, $p < .001$). In addition, a low correlation was found between first sit and first steps ($r = .296$, $p < .001$).

Sex differences in infant movement activity level and developmental milestones

Infant movement activity level was higher in boys ($M = 2.38$, $SD = 0.72$) than girls ($M = 2.31$, $SD = .72$; p for difference $< .001$), although the effect size was small ($d = 0.097$). Age at first sit was slightly earlier in boys ($M = 7.36$ months, $SD = 1.51$) than in girls ($M = 7.54$ months, $SD = 1.61$; $p < .001$), also with a small effect size ($d = 0.115$). Age at first crawl and age at first steps were not significantly different between the sexes. Genetic and environmental estimates were broadly similar for boys and girls (data available from the corresponding author); therefore, analyses are presented using whole-group data.

Analyses of genetic and environmental influences

Within-pair ICCs for infant movement activity level and developmental milestones are presented in Figure 1. MZ correlations were higher than DZ correlations for all outcomes, indicating genetic influence. DZ correlations were more than half the MZ correlations for infant movement activity level, first sit, and first crawl, indicating a shared environment effect. The DZ correlation was around half that of the MZ correlation for first steps, indicating strong genetic influence.

Quantitative estimates (full models presented in Table 3) confirmed the indications from the ICCs. The best-fitting model for infant movement activity level was the full ACE model; with genes explaining 48% of the variance and the shared environment explaining 45%. A small percentage (7%) of variance was explained by the unique environment plus measurement error. Similarly, the age when children could sit unsupported was significantly influenced by

genes (48%) and the shared environment (42%), with a small contribution (10%) from the unique environment. The heritability estimate for the age when children first crawled was similar (54%), with contributions from shared (33%) and unique (13%) environments. The more parsimonious AE model was the best fit for first steps, indicating that 84% of the variance was explained by genes with no detectable effect of the shared environment.

Based on these parameters, power to detect a shared environment effect at $\alpha = .05$ for movement activity, first crawl, and first sit was 100%. For first steps, power to detect a significant shared environment effect was slightly lower because the sample size was smaller, but the power to detect a significant shared environmental effect of 17% (the upper bound of the CI observed in the quantitative analyses) was 100%. There was no evidence of contrast effects in our data.

Discussion

The results of this study indicate the environment has an important role in infant movement activity level and motor development, although genetic factors dominate the emergence of walking (first steps). The magnitude of the genetic effect on movement activity level in our study (around 48%) was very similar to that observed in smaller twin studies using the IBQ Activity subscale 15 or objective measures (Saudino & Eaton, 1991, 1995). It is unclear whether infant movement activity (movement of arms and legs) maps on to “fidgeting,” which also demonstrates high heritability (Fisher, van Jaarsveld, Llewellyn, & Wardle, 2010), or if it is more related to play behavior (Saudino &

Zapfe, 2008). Relationships between these childhood activity behaviors warrant future research.

Finding a significant shared environment effect raises the interesting question of which specific environmental factors are responsible. Parental intervention may play an important role at this stage of life—for example, coaxing babies to wave their arms in response to a toy or encouraging them to practice sitting. Aspects of the psychosocial environment (e.g., parental encouragement and modeling) are known to affect childhood activity levels (Hinkley, Crawford, Salmon, Okely, & Hesketh, 2008), and they may also be important in infancy. Preschool children with more siblings tend to be more active (Hesketh, Crawford, & Salmon, 285 2006), perhaps because infants try to copy the movements of their older siblings. Similarly, older siblings can influence motor development by providing more interaction (Berger & Nuzzo, 2008). Availability of age appropriate toys or parental knowledge of expected developmental milestones may also affect motor development. However, parents also encourage walking, and we found no evidence for any shared environmental influence, suggesting that family effects for the other milestones are likely to be more than mere encouragement.

One possibility is that the key parental influences are not related to advancing motor milestones but to retarding them. The available literature has indicated that children need to be as active and free as possible for adequate motor development. For example, they must develop the strength required to push against gravity required in the development of sitting (Tecklin, 2008). Use of

devices such as infant walkers, swings, bouncers, and car seats may have a negative impact on early motor development (Tecklin, 2008), and reaching developmental milestones is universally later now than it was previous years (Piek, 2006). This finding could be a product of an increasingly sedentary population with more access to such devices. At present, we do not know whether they influence development of physical activity behavior and preferences, but it is a possibility.

A survey of 400 pediatric occupational therapists expressed the view that modern infants spend too long on their backs (e.g., in car seats that can be removed and attached directly to strollers or swings; Pathways, 2011). While parents are generally aware of the recommendation by the American Academy of Pediatrics (AAP) Task Force on Infant Positioning and SIDS (1992) to place infants on their backs when sleeping, fewer caregivers are aware of the “prone to play” message, which encourages parents to place infants on their fronts during waking time for optimal early motor development (Zachry et al., 2011). There is evidence that some parents purposely place infants on their backs even when awake due to a misconception that it will reduce the incidence of sudden infant death syndrome (Zachry et al., 2011). Parents may need to be more clearly informed that the “back to Sleep” and “prone to lay” messages advocated by AAP are complementary rather than contradictory. Interestingly, a longitudinal cohort study revealed that prone time only influenced early motor milestones (including crawling and sitting) and did not influence first steps (Kuo, Liao, Chen, Hsieh, & Hwang, 2008). This finding is consistent with our finding that the shared environment was

significant for earlier milestones but not for walking. In further support of a shared environment effect, a number of modifiable factors that influence achievement of developmental milestones have already been identified—for example, maternal smoking during pregnancy and in the 1st year predicts developmental delay (Slykerman et al., 2007). Breastfeeding is highly beneficial for motor development and may influence infant activity (Worobey, 1998). Children from lower socioeconomic groups are more likely to be more developmentally delayed (Bradley & Corwyn, 2002), and the childcare setting can also influence age of achievement of milestones (Mulligan, Specker, Donna, O'Connor, & Ho, 1998).

One study showed no genetic influence on sitting without support but did show significant genetic influence on crawling and first steps (> 90%). However, the small sample size meant that CIs included 0, so it is difficult to draw conclusions (Goetghebuer et al., 2003). In their sample of twins and siblings, Peter et al. (1999) found that the shared environment explained more than 50% of the variance in sitting unsupported and walking. Our results support these estimates for sitting, but we found that genetic factors explained most of the variance in first walking unaided. Different measures could contribute to the differences, as Peter et al. asked when infants could walk at least five steps unsupported, whereas we asked about first walking unaided. However, it is more likely a sample-size effect.

In support of our findings of genetic influences, motor development and skill level are likely to be influenced by factors such as muscle-fiber type and

mitochondrial activity, which, although trainable, are partly genetically determined (Mulligan et al., 1998). There have been few studies of specific genes that influence motor activity level, although the dopamine system is implicated in motor activity. For example, infants with the long allele of the dopamine receptor DRD4 showed higher motor activity (Auerbach et al., 2001).

Our study is the largest to date to examine genetic and environmental influences on infant motor development, and it has the statistical power to generate good estimates of both environmental and genetic parameters. The large sample size meant that we were reliant on parental reports rather than objective measures, but the error term was not strikingly high and there was little evidence in our data of contrast bias (parents overestimating differences between DZ twins and underestimating MZ differences; Saudino, Cherny, & Plomin, 2000). Although our genetic estimates for infant activity level are similar to previous studies, finding a strong shared (as opposed to unique) environment effect is novel (Goldsmith & Campos, 1999; Saudino, 2005; Saudino & Eaton, 1991). It is possible that use of parental retrospective recall of infant activity inflated the shared environment estimate. However, it is also possible that the environment has changed since these earlier studies and that parental and societal patterns are exerting stronger effects. Twins attain their developmental milestones slightly later than do singletons, although a study comparing 2,151 twin pairs and 2,151 singletons revealed no significant differences in age when reaching five developmental milestones (turn, sit,

crawl, stand, and walk) within the normal range (Brouwer, van Beijsterveldt, Bartels, Hudziak, & Boomsma, 2006). There is no reason to suppose that the magnitude of genetic and environmental influences would differ between twins and singletons. In our sample, a proportion of infants had not begun walking by the time the 15-month questionnaire was returned; therefore, our results may not be fully generalizable to late-developing infants.

Conclusions

Genes are significant determinants of early-life motor activity and developmental motor milestones, but the environment also plays an important role. These results support the need for research to identify the specific genes and specific environmental factors that influence motor development.

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Table 1. Participant characteristics

Characteristics	MZ	n	DZ	n	Cohen's d
	Mean (SD)		Mean (SD)		
Gestational age (weeks)	35.59 (2.52)		36.48 (2.40)		0.362
Female (%)	52.7		49.7		
Infant activity level (IBQ-R)	2.34 (0.73)	1425	2.34 (0.71)	3130	0.000
First sit (age reached months; range 3-15)	7.68 (1.63)	1247	7.34 (1.52)	2705	0.216
First crawl (age reached months; range 3-19)	9.51 (1.98)	1174	9.25 (1.92)	2502	0.133
First steps (age reached months; range 6-20)	13.13 (1.69)	868	13.04 (1.57)	1976	0.055

Note. MZ = monozygotic twins; DZ = dizygotic twins; n = number of infants in the sample with complete data for analyses.

Table 2. Correlations between infant activity level and developmental milestones

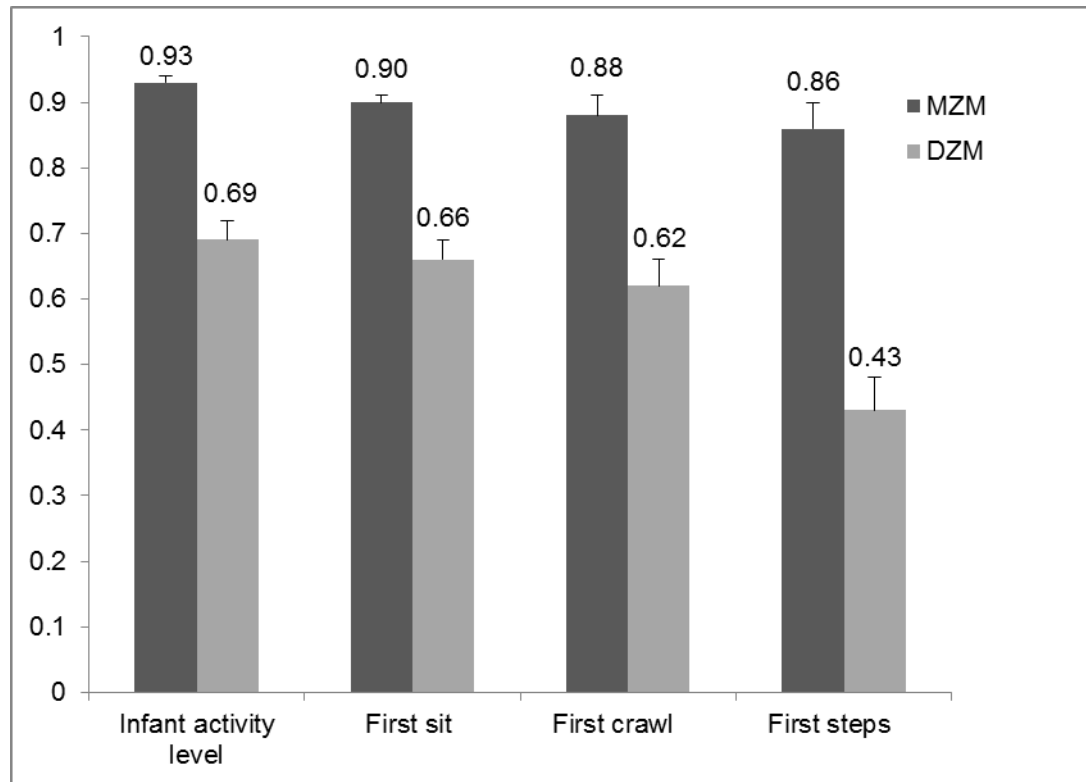
	First sit	First crawl	First steps
Infant activity level	-0.168**	-0.212**	-0.135**
First sit	-	0.468**	0.296**
First crawl	-	-	0.476**

**p<0.001 Data are partial correlation coefficients (adjusting for gestational age)

AL: activity level at 3 months: mean score from the activity subscale of the Revised Infant Behaviour Questionnaire (IBQ-R) where higher scores = more active children.

First sit unaided, first crawl and first steps are age first observed in months as reported by parents.

FIGURE 1. Intraclass correlations (and 95% confidence intervals) between MZ and DZ twin pairs for developmental milestones and infant activity level.



Activity level from the Revised Infant Behaviour Questionnaire activity level subscale. First crawl, First sit, First steps=age in months when infants could first crawl, sit up unaided and take first steps unaided reported by parent. MZ=monozygotic twins DZ= dizygotic twins. Data are regressed on gestational age, age of questionnaire completion and sex.

Table 3. Genetic and environmental influences on infant activity level and developmental milestones in the Gemini birth cohort

Model	Estimates of variance components						Model fit		
		a ²	c ²	e ²	-2LL	df	ΔAIC	Δ x ²	p
Infant AL	ACE [†]	0.48 (0.43, 0.53)	0.45 (0.40, 0.50)	0.07 (0.06, 0.08)	10482.111	4548	-	-	-
	CE	-	0.77 (0.75, 0.78)	0.23 (0.22, 0.25)	10910.577	4549	426.466	428.466	<0.001
	AE	0.93 (0.92, 0.93)	-	0.07 (0.07, 0.08)	10675.108	4549	190.997	192.997	<0.001
	E	-	-	1.00	12934.658	4550	2447.306	2451.306	<0.001
First sit	ACE [†]	0.48 (0.42, 0.54)	0.42 (0.36, 0.48)	0.10 (0.09, 0.12)	6096.595	3735	-	-	-
	CE	-	0.73 (0.71, 0.75)	0.27 (0.25, 0.29)	6344.966	3736	246.371	248.371	<0.001
	AE	0.90 (0.88, 0.91)	-	0.10 (0.09, 0.11)	6222.905	3736	124.310	126.310	<0.001
	E	-	-	1.00	7795.355	3737	1694.759	1698.759	<0.001
First crawl	ACE [†]	0.54 (0.47, 0.62)	0.33 (0.26, 0.40)	0.13 (0.11, 0.15)	8603.895	3497	-	-	-
	CE	-	0.69 (0.66, 0.71)	0.31 (0.29, 0.34)	8812.538	3498	206.643	208.643	<0.001
	AE	0.87 (0.86, 0.89)	-	0.13 (0.11, 0.14)	8663.870	3498	57.975	57.975	<0.001
	E	-	-	1.00	8603.895	3497	1289.205	1293.205	<0.001
First steps	ACE	0.77 (0.66, 0.86)	0.07 (0.00, 0.17)	0.16 (0.14, 0.19)	7314.302	2825	-	-	-
	CE	-	0.59 (0.55, 0.62)	0.41 (0.38, 0.45)	7496.604	2826	180.303	182.303	<0.0001
	AE [†]	0.84 (0.81, 0.86)	-	0.16 (0.14, 0.19)	7316.022	2826	-0.280	1.720	0.190
	E	-	-	1.00	8042.953	2827	724.651	728.651	<0.001

[†] Best fitting model; A=additive genetic; C=shared environment ; E=unique environment / measurement error. AL; activity